

WHAT IS CLAIMED IS:

1. A method of treating a patient suffering from increased urinary urge, increased micturition frequency, urinary incontinence, urge incontinence, overactive bladder or stress-induced incontinence, said method comprising administering a pharmaceutically effective amount of buprenorphine using a transdermal delivery system wherein said transdermal delivery system maintains mean relative release rates over a dosing interval as follows:

a mean relative release rate of from about 3 µg per hr to about 86 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 0.3 µg per hr to about 9 µg per hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

2. The method of claim 1, wherein said transdermal delivery system remains in contact with a patient's skin for an at least five-day dosing interval, and maintains: a substantially first order plasma level increase of buprenorphine from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and a substantially zero order plasma level fluctuation of buprenorphine from about 72 hours after the initiation of the dosing interval until the end of the dosing interval, such that the following mean plasma

concentrations are achieved:

a mean plasma concentration from about 0.3 to about 113 pg per ml
at about 6 hours after initiation of the dosing interval;

a mean plasma concentration from about 3 to about 296 pg per ml
at about 12 hours after initiation of the dosing interval;

a mean plasma concentration from about 7 to about 644 pg per ml
at about 24 hours after initiation of the dosing interval;

a mean plasma concentration from about 13 to about 753 pg per ml
at about 36 hours after initiation of the dosing interval;

a mean plasma concentration from about 16 to about 984 pg per ml
at about 48 hours after initiation of the dosing interval;

a mean plasma concentration from about 20 to about 984 pg per ml
at about 60 hours after initiation of the dosing interval;

a mean plasma concentration from about 21 to about 1052 pg per ml
at about 72 hours after initiation of the dosing interval; and

a mean plasma concentration from about 19 to about 1052 pg per ml
over at least the next 48 hours.

3. The method of claim 2, wherein the mean plasma concentrations
are further maintained as follows:

a mean plasma concentration from about 23 to about 1052 pg per ml at about 96 hours after initiation of the dosing interval;

a mean plasma concentration from about 23 to about 1052 pg per ml at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 22 to about 970 pg per ml at about 144 hours after initiation of the dosing interval; and

a mean plasma concentration from about 19 to about 841 pg per ml at about 168 hours after initiation of the dosing interval.

4. The method of claim 3 wherein the plasma level of buprenorphine at 72 hours does not decrease by more than 30% over the next 48 hours.

5. The method of claim 3 wherein the plasma level of buprenorphine at 120 hours does not decrease by more than 30% over the next 48 hours.

6. The method of claim 2, wherein said transdermal delivery system maintains a mean relative release rate of from about 13 µg per hr to about 21 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval, and a mean relative release rate of about 1 µg per hr to about 2 µg per hr from about 72 hours after the initiation of the dosing

interval until the end of at least the five-day dosing interval, such that the following mean plasma concentrations are achieved:

a mean plasma concentration from about 1 to about 28 pg per ml at about 6 hours after initiation of the dosing interval;

a mean plasma concentration from about 14 to about 74 pg per ml at about 12 hours after initiation of the dosing interval;

a mean plasma concentration from about 30 to about 161 pg per ml at about 24 hours after initiation of the dosing interval;

a mean plasma concentration from about 51 to about 188 pg per ml at about 36 hours after initiation of the dosing interval;

a mean plasma concentration from about 62 to about 246 pg per ml at about 48 hours after initiation of the dosing interval;

a mean plasma concentration from about 79 to about 246 pg per ml at about 60 hours after initiation of the dosing interval;

a mean plasma concentration from about 85 to about 263 pg per ml at about 72 hours after initiation of the dosing interval; and

a mean plasma concentration from about 77 to about 263 pg per ml over at least the next 48 hours.

7. The method of claim 6, wherein the mean plasma concentrations

are further maintained as follows:

a mean plasma concentration from about 92 to about 263 pg per ml at about 96 hours after initiation of the dosing interval;

a mean plasma concentration from about 94 to about 263 pg per ml at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 86 to about 243 pg per ml at about 144 hours after initiation of the dosing interval; and

a mean plasma concentration from about 77 to about 210 pg per ml at about 168 hours after initiation of the dosing interval.

8. The method of claim 2, wherein said transdermal delivery system maintains a mean relative release rate of from about 3 µg per hr to about 5 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval, and a mean relative release rate of about 0.3 µg per hr to about 0.6 µg per hr from about 72 hours after the initiation of the dosing interval until the end of at least the five-day dosing interval, such that the following mean plasma concentrations are achieved:

a mean plasma concentration from about 0.3 to about 7 pg per ml at about 6 hours after initiation of the dosing interval;

a mean plasma concentration from about 4 to about 19 pg per ml at

about 12 hours after initiation of the dosing interval;

a mean plasma concentration from about 7 to about 40 pg per ml at

about 24 hours after initiation of the dosing interval;

a mean plasma concentration from about 13 to about 47 pg per ml

at about 36 hours after initiation of the dosing interval;

a mean plasma concentration from about 16 to about 62 pg per ml

at about 48 hours after initiation of the dosing interval;

a mean plasma concentration from about 20 to about 62 pg per ml

at about 60 hours after initiation of the dosing interval;

a mean plasma concentration from about 21 to about 66 pg per ml

at about 72 hours after initiation of the dosing interval; and

a mean plasma concentration from about 19 to about 66 pg per ml

over at least the next 48 hours.

9. The method of claim 8, wherein the mean plasma concentrations are further maintained as follows:

a mean plasma concentration from about 23 to about 66 pg per ml

at about 96 hours after initiation of the dosing interval;

a mean plasma concentration from about 23 to about 66 pg per ml

at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 22 to about 61 pg per ml at about 144 hours after initiation of the dosing interval; and
a mean plasma concentration from about 19 to about 53 pg per ml at about 168 hours after initiation of the dosing interval.

10. The method of claim 2, wherein said transdermal delivery system maintains a mean relative release rate of from about 6 µg per hr to about 11 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval, and a mean relative release rate of about 0.7 µg per hr to about 1 µg per hr from about 72 hours after the initiation of the dosing interval until the end of at least the five-day dosing interval, such that the following mean plasma concentrations are achieved:

a mean plasma concentration from about 0.7 to about 14 pg per ml at about 6 hours after initiation of the dosing interval;
a mean plasma concentration from about 7 to about 37 pg per ml at about 12 hours after initiation of the dosing interval;
a mean plasma concentration from about 15 to about 80 pg per ml at about 24 hours after initiation of the dosing interval;
a mean plasma concentration from about 25 to about 94 pg per ml at about 36 hours after initiation of the dosing interval;

a mean plasma concentration from about 31 to about 123 pg per ml at about 48 hours after initiation of the dosing interval;

a mean plasma concentration from about 40 to about 123 pg per ml at about 60 hours after initiation of the dosing interval;

a mean plasma concentration from about 42 to about 132 pg per ml at about 72 hours after initiation of the dosing interval; and

a mean plasma concentration from about 38 to about 132 pg per ml over at least the next 48 hours.

11. The method of claim 10, wherein the mean plasma concentrations are further maintained as follows:

a mean plasma concentration from about 46 to about 132 pg per ml at about 96 hours after initiation of the dosing interval;

a mean plasma concentration from about 47 to about 132 pg per ml at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 43 to about 121 pg per ml at about 144 hours after initiation of the dosing interval; and

a mean plasma concentration from about 38 to about 105 pg per ml at about 168 hours after initiation of the dosing interval.

12. The method of claim 2, wherein said transdermal delivery system maintains a mean relative release rate of from about 26 µg per hr to about 43 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval, and a mean relative release rate of about 2 µg per hr to about 4 µg per hr from about 72 hours after the initiation of the dosing interval until the end of at least the five-day dosing interval, such that the following mean plasma concentrations are achieved:

a mean plasma concentration from about 3 to about 57 pg per ml at about 6 hours after initiation of the dosing interval;

a mean plasma concentration from about 28 to about 148 pg per ml at about 12 hours after initiation of the dosing interval;

a mean plasma concentration from about 59 to about 322 pg per ml at about 24 hours after initiation of the dosing interval;

a mean plasma concentration from about 102 to about 377 pg per ml at about 36 hours after initiation of the dosing interval;

a mean plasma concentration from about 124 to about 492 pg per ml at about 48 hours after initiation of the dosing interval;

a mean plasma concentration from about 159 to about 492 pg per ml at about 60 hours after initiation of the dosing interval;

a mean plasma concentration from about 169 to about 526 pg per ml

at about 72 hours after initiation of the dosing interval; and

a mean plasma concentration from about 153 to about 526 pg per ml over at least the next 48 hours.

13. The method of claim 12, wherein the mean plasma concentrations are further maintained as follows:

a mean plasma concentration from about 184 to about 526 pg per ml at about 96 hours after initiation of the dosing interval;

a mean plasma concentration from about 187 to about 526 pg per ml at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 173 to about 485 pg per ml at about 144 hours after initiation of the dosing interval; and

a mean plasma concentration from about 153 to about 420 pg per ml at about 168 hours after initiation of the dosing interval.

14. The method of claim 2, wherein said transdermal delivery system maintains a mean relative release rate of from about 38 µg per hr to about 64 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval, and a mean relative release rate of about 4 µg per hr to about 7 µg per hr from about 72 hours after the initiation of the dosing

interval until the end of at least the five-day dosing interval, such that the following mean plasma concentrations are achieved:

a mean plasma concentration from about 4 to about 85 pg per ml at about 6 hours after initiation of the dosing interval;

a mean plasma concentration from about 42 to about 222 pg per ml at about 12 hours after initiation of the dosing interval;

a mean plasma concentration from about 89 to about 483 pg per ml at about 24 hours after initiation of the dosing interval;

a mean plasma concentration from about 152 to about 565 pg per ml at about 36 hours after initiation of the dosing interval;

a mean plasma concentration from about 186 to about 738 pg per ml at about 48 hours after initiation of the dosing interval;

a mean plasma concentration from about 238 to about 738 pg per ml at about 60 hours after initiation of the dosing interval;

a mean plasma concentration from about 254 to about 789 pg per ml at about 72 hours after initiation of the dosing interval; and

a mean plasma concentration from about 230 to about 789 pg per ml over at least the next 48 hours.

15. The method of claim 14, wherein the mean plasma concentrations

are further maintained as follows:

a mean plasma concentration from about 276 to about 789 pg per ml at about 96 hours after initiation of the dosing interval;

a mean plasma concentration from about 281 to about 789 pg per ml at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 259 to about 727 pg per ml at about 144 hours after initiation of the dosing interval; and

a mean plasma concentration from about 230 to about, 630 pg per ml at about 168 hours after initiation of the dosing interval.

16. The method of claim 2, wherein said transdermal delivery system maintains a mean relative release rate of from about 51 µg per hr to about 86 µg per hr from initiation of the dosing interval until about 72 hours after the initiation of the dosing interval, and a mean relative release rate of about 5 µg per hr to about 9 µg per hr from about 72 hours after the initiation of the dosing interval until the end of at least the five-day dosing interval, such that the following mean plasma concentrations are achieved:

a mean plasma concentration from about 5 to about 113 pg per ml at about 6 hours after initiation of the dosing interval;

a mean plasma concentration from about 55 to about 296 pg per ml

at about 12 hours after initiation of the dosing interval;
a mean plasma concentration from about 118 to about 644 pg per ml
at about 24 hours after initiation of the dosing interval;
a mean plasma concentration from about 203 to about 753 pg per ml
at about 36 hours after initiation of the dosing interval;
a mean plasma concentration from about 247 to about 984 pg per ml
at about 48 hours after initiation of the dosing interval;
a mean plasma concentration from about 317 to about 984 pg per ml
at about 60 hours after initiation of the dosing interval;
a mean plasma concentration from about 339 to about 1052 pg per ml at about 72 hours after initiation of the dosing interval; and
a mean plasma concentration from about 306 to about 1052 pg per ml over at least the next 48 hours.

17. The method of claim 16, wherein the mean plasma concentrations are further maintained as follows:

a mean plasma concentration from about 369 to about 1052 pg per ml at about 96 hours after initiation of the dosing interval;
a mean plasma concentration from about 374 to about 1052 pg per ml at about 120 hours after initiation of the dosing interval;

a mean plasma concentration from about 346 to about 970 pg per ml at about 144 hours after initiation of the dosing interval; and

a mean plasma concentration from about 306 to about 841 pg per ml at about 168 hours after initiation of the dosing interval.

18. The method of claim 1, wherein the mean relative release rates achieved over the dosing interval are as follows:

a mean relative release rate of from about 3 µg per hr to about 5 µg per hr from the initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 0.3 µg per hr to about 0.6 µg per hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

19. The method of claim 1, wherein the mean relative release rates achieved over the dosing interval are as follows:

a mean relative release rate of from about 6 µg per hr to about 11 µg per hr from the initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 0.7 µg per hr to about 1 µg per

hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

20. The method of claim 1, wherein the mean relative release rates achieved over the dosing interval are as follows:

a mean relative release rate of from about 13 µg per hr to about 21 µg per hr from the initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 1 µg per hr to about 2 µg per hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

21. The method of claim 1, wherein the mean relative release rates achieved over the dosing interval are as follows:

a mean relative release rate of from about 26 µg per hr to about 43 µg per hr from the initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 3 µg per hr to about 4 µg per hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

22. The method of claim 1, wherein the mean relative release rates achieved over the dosing interval are as follows:

a mean relative release rate of from about 39 µg per hr to about 64 µg per hr from the initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 4 µg per hr to about 7 µg per hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

23. The method of claim 1, wherein the mean relative release rates achieved over the dosing interval are as follows:

a mean relative release rate of from about 51 µg per hr to about 86 µg per hr from the initiation of the dosing interval until about 72 hours after the initiation of the dosing interval; and

a mean relative release rate of about 5 µg per hr to about 9 µg per hr from about 72 hours after the initiation of the dosing interval until the end of the dosing interval.

24. A method of treating a patient suffering from increased urinary

urge, increased micturition frequency, urinary incontinence, urge incontinence, overactive bladder or stress-induced incontinence in a mammal, said method comprising administering a pharmaceutically effective amount of buprenorphine using a transdermal delivery system wherein said transdermal delivery system maintains a substantially first order plasma level increase of buprenorphine over a first three-day dosing interval, such that a mean plasma concentration from about 21 to about 1052 pg per ml is attained at about 72 hours after application of said transdermal delivery system, and maintains for at least an additional two-day dosing interval a mean relative release rate from about 0.3 μ g per hr to about 9 μ g per hr.

25. The method of claim 24, wherein from about 68% to about 95% of the buprenorphine is contained in the transdermal delivery system at the end of the dosing interval.

26. The method of claim 24, wherein the T_{max} occurs from about 3 to about 5 days after application of said transdermal delivery system.

27. The method of claim 24, wherein the mean plasma concentration attained about 72 hours after application of said transdermal delivery system is from about 85 to about 263 pg per ml; and the mean relative release rate

maintained over said at least two-day additional dosing interval is from about 13 µg per hr to about 21 µg per hr.

28. The method of claim 24, wherein the mean plasma concentration attained about 72 hours after application of said transdermal delivery system is from about 21 to about 66 pg per ml; and the mean relative release rate maintained over said at least two-day additional dosing interval is from about 0.3 µg per hr to about 0.6 µg per hr.

29. The method of claim 24, wherein the mean plasma concentration attained about 72 hours after application of said transdermal delivery system is from about 42 to about 132 pg per ml.

30. The method of claim 24, wherein the mean plasma concentration attained about 72 hours after application of said transdermal delivery system is from about 169 to about 526 pg per ml; and the mean relative release rate maintained over said at least two-day additional dosing interval is from about 3 µg per hr to about 4 µg per hr.

31. The method of claim 24, wherein the mean plasma concentration

attained about 72 hours after application of said transdermal delivery system is from about 254 to about 789 pg per ml; and the mean relative release rate maintained over said at least two-day additional dosing interval is from about 4 µg per hr to about 7 µg per hr.

32. The method of claim 24, wherein the mean plasma concentration attained about 72 hours after application of said transdermal delivery system is from about 339 to about 1052 pg per ml; and the mean relative release rate maintained over said at least two-day additional dosing interval is from about 5 µg per hr to about 9 µg per hr.

33. The method of claim 1, wherein said buprenorphine is in the form of a stereoisomer, enantiomer, diastereoisomer, or a mixture of the foregoing.

34. The method of claim 1, wherein said buprenorphine is in the form of a racemic mixture.

35. The method of claim 1, wherein said buprenorphine is in the form of a salt, solvate, hydrate, or a mixture of the foregoing.

36. The method of claim 1, wherein said buprenorphine is in the form of a free base.

37. The method of claim 24, wherein said buprenorphine is in the form of a stereoisomer, enantiomer, diastereoisomer, or a mixture of the foregoing.

38. The method of claim 24, wherein said buprenorphine is in the form of a racemic mixture.

39. The method of claim 24, wherein said buprenorphine is in the form of a salt, solvate, hydrate, or a mixture of the foregoing.

40. The method of claim 24, wherein said buprenorphine is in the form of a free base.